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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,986	04/20/2004	Michael T. Barrett	10031482-1	7617

22878 7590 06/08/2006

AGILENT TECHNOLOGIES, INC.
INTELLECTUAL PROPERTY ADMINISTRATION, LEGAL DEPT.
P.O. BOX 7599
M/S DL429
LOVELAND, CO 80537-0599

EXAMINER	
SHAW, AMANDA MARIE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/828,986	BARRETT ET AL.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *7-24 and 30-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I in the reply filed on May 9, 2006 is acknowledged. Accordingly, Claims 1-6 and 25-29 have been examined herein.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 25-29 are indefinite over the recitation of the phrase "CpG unstructured nucleic acid". This phrase is defined in the specification as a oligonucleotide that a) contains at least one UNA nucleotide and therefore has reduced secondary structure and b) corresponds to i.e. has a sequences that is at least partially complementary to or the same as and will base pair with a CpG island. This definition is indefinite because it is not clear as to what is meant by partially complementary. For example it could mean that the oligonucleotide can contain just one CpG site or a sequence that shares complementary with a CpG site or the definition could mean that the oligonucleotide comprises a sequence that is at least of the same length as a CpG island and which is fully complementary to the CpG island or shares any level (>1%) etc level of complementary to the CpG island such that the oligo hybridizes to the CpG island under any hybridization conditions.

Claims 5 –6 and 27 are indefinite over the recitation of the phrase "an array of features". This phrase in considered unclear because "an array of features" is not clearly defined in the specification and there is no art recognized definition for this phrase. For example, it is unclear as to whether "an array of features" refers to an array containing DNA, RNA, polypeptides, or tissue samples.

Claim 28 is objected to because a claim to a product does not properly depend from a claim to a method that can be used to obtain instructions (i.e., "instructions for performing the methods of claim 7 or 15)." As stated in MPEP 608.01(n), "The test as to whether a claim is a proper dependent claim is that it shall include every limitation of the claim from which it depends (35 U.S.C. 112, fourth paragraph) or in other words that it shall not conceivably be infringed by anything which would not also infringe the basic claim... On the other hand, if claim 1 recites a method of making a specified product, a claim to the product set forth in claim 1 would not be a proper dependent claim since it is conceivable that the product claim can be infringed without infringing the base method claim." In the present situation, the kit of claim 28 does not include every limitation of the claim from which it depends (i.e., claim 7 or 15) because claim 28 does not require performing the method steps recited in claims 7 or 15.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Kutyavin et al (US Patent 5912340).

For the following rejections a CpG UNA oligonucleotide is being interpreted as: a) an oligonucleotide which contains at least one UNA nucleotide and therefore has reduced secondary structure and b) an oligonucleotide which contains at least one **CpG site** or a or a sequence that shares complementarity with a **CpG site.**

Regarding Claim 1 Kutyavin et al teach unstructured CpG specific probes (See Table 2). This is considered a unstructured CpG specific probes because the probe contains at least one UNA nucleotide and therefore has reduced secondary structure and b) an oligonucleotide which contains at least one CpG site or a or a sequence that shares complementary with a CpG site.

Regarding Claim 3 Kutyavin et al teach probes which comprises nucleotides G' (6-oxo-purine (hypoxanthine)) and C' (pyrrolo-[2,3-d]pyrimidine-2(3H) wherein said nucleotides G' and C' base pair with each other with a stability that is lower than that of G and C. All of the probes of the present invention are capable of forming stable base pairs with their natural partner base, but not with their modified partner. (Abstract, Columns 7 and 8).

Regarding Claim 4 Kutyavin et al teach probes which comprise nucleotides A' (2-aminoadenine) and T' (2-thiothymine) wherein said nucleotides A' and T' base pair with each other with a stability that is lower than that of A and T. All of the probes of the

present invention are capable of forming stable base pairs with their natural partner base, but not with their modified partner. (Abstract, Columns 6 and 7).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

For the following rejections a CpG UNA oligonucleotide is being interpreted as: a) an oligonucleotide which contains at least one UNA nucleotide and therefore has reduced secondary structure and b) an oligonucleotide which contains atleast one **CpG site** or a or a sequence that shares complementarity with a **CpG site.**

Claims 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kutyavin et al (US Patent 5912340) in view of Laird (US Patent 6331393).

The teachings of Kutyavin et al are presented above.

Kutyavin et al do not teach a CpG nucleotide which can distinguish between unmethylated and methylated nucleic acids.

However Laird et al teaches the concept of CpG specific probes that can distinguish between unmethylated and methylated nucleic acids (Column 5). In the instant case uncleaved CpG islands are being interpreted methylated CpG islands and cleaved CpG islands are being interpretated as unmethylated CpG islands.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the probes taught by Kutyavin so that they can distinguish between unmethylated and methylated nucleic acids in order for a more effective way to detect CpG sites.

5. Claims 5-6 and 26-28 rejected under 35 U.S.C. 103(a) as being unpatentable over Kutyavin et al (US Patent 5912340) in view of Fodor (US Patent 5800992).

The teachings of Kutyavin et al are presented above.

Regarding Claims 5 and 6 Kutyavin et al do not teach an array containing at least 1000 different CPG UNA oligonucleotides.

However Fodor et al teaches the concept of arrays which comprise a plurality of nucleic acid sequences attached to assigned locations on a solid substrate. Fodor et al teaches that there can be about 3000 different sequences on the array (Columns 2 and 3). Fodor teaches that this methodology provides a rapid, reliable, less expensive and automatable means for reproducibly and accurately analyzing nucleic acid samples (Column 2).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have attached the probes of Laird to an array because the array methods of Fodor provides a rapid, reliable, less expensive and automatable means for reproducibly and accurately analyzing nucleic acid samples.

Regarding Claims 25-29 Kutyavin et al do not teach a kit containing an array of CPG UNA oligonucleotides.

However Fodor et al teaches the concept of packaging arrays in kits. Specifically Fodor et al teach that the kits contain various compartments with the desired necessary reagents, e.g., substrate, labeling reagents for target samples, buffers, and other useful accompanying products (Column 60). Additionally it would be obvious to include instructions on how to use the kit.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have packaged the array of probes into a kit. Reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the array of probes in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art wishing to perform hybridization reactions.

6. For the following rejections a CpG UNA oligonucleotide is being interpreted as: a) an oligonucleotide which contains at least one UNA nucleotide and therefore has reduced secondary structure and b) an oligonucleotide which is specific for **CpG islands**.

Claims 1-4, and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laird et al (US Patent 6331393) in view of Kutyavin et al (US Patent 5912340).

Laird et al teach the concept of CpG specific probes that can distinguish between unmethylated and methylated nucleic acids (Column 5).

However Laird et al do not teach the concept of nucleic acid probes which comprise unnatural occurring base pairs

However, Kutyavin et al teach the concept of nucleic acid probes which comprise unnatural occurring base pairs which are capable of forming stable base pairs with their natural partner base, but not with their modified partner. This is accomplished when in a hybridized structure the modified base is capable of forming two or more hydrogen bonds with its natural complementary base, but only one hydrogen bond with its modified partner. As a result the nucleic acid molecules which have unnatural bases have less secondary structure compared to nucleic acids with naturally occurring bases.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the probes taught by Laird by incorporating unnatural bases for the detection of CpG sites because the probes of Kutyavin allow for the reduction of the formation of secondary structures between adjacent probes which can block the hybridization of the target to the probes. Thereby, modifying the probes of Laird would have allowed for a more effective means for detecting CpG islands.

Regarding Claim 2 Laird et al teaches the concept of CpG specific probes that can distinguish between unmethylated and methylated nucleic acids (Column 5). In the instant case uncleaved CpG islands are being interpreted methylated CpG islands and cleaved CpG islands are being interpretated as unmethylated CpG islands.

Regarding Claim 3 Laird et al does not teach probes which comprise nucleotides G' and C' wherein said nucleotides G' and C' base pair with each other with a stability that is lower than that of G and C. However Kutyavin et al teach probes which comprise nucleotides G' (6-oxo-purine (hypoxanthine)) and C' (pyrrolo-[2,3-d]pyrimidine-2(3H) wherein said nucleotides G' and C' base pair with each other with a stability that is lower than that of G and C. All of the probes of the present invention are capable of forming stable base pairs with their natural partner base, but not with their modified partner. (Abstract, Columns 7 and 8).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the probes taught by Laird by incorporating unnatural bases for the detection of CpG sites because the probes of Kutyavin allow for the reduction of the formation of secondary structures between adjacent probes which can block the hybridization of the target to the probes. Thereby, modifying the probes of Laird would have allowed for a more effective means for detecting CpG islands.

Regarding Claim 4 Laird et al does not teach probes which comprise nucleotides A' and T' wherein said nucleotides A' and T' base pair with each other with a stability that is lower than that of A and T. However Kutyavin et al teach probes which comprise nucleotides A' (2-aminoadenine) and T' (2-thiothymine) wherein said nucleotides A' and T' base pair with each other with a stability that is lower than that of A and T. All of the probes of the present invention are capable of forming stable base pairs with their natural partner base, but not with their modified partner. (Abstract, Columns 6 and 7).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the probes taught by Laird by incorporating unnatural bases for the detection of CpG sites because the probes of Kutyavin allow for the reduction of the formation of secondary structures between adjacent probes which can block the hybridization of the target to the probes. Thereby, modifying the probes of Laird would have allowed for a more effective means for detecting CpG islands.

Regarding Claims 25 and 29, Laird et al teach a kit containing CpG specific probes that can distinguish between unmethylated and methylated nucleic acids wherein the probes further comprise a fluorescent moiety (Column 6).

7. Claims 5-6 and 26-28 rejected under 35 U.S.C. 103(a) as being unpatentable over Laird et al (US Patent 6331393) in view of Kutyavin et al (US Patent 5912340) and in further view of Fodor (US Patent 5800992).

The teachings of Laird et al and Kutyavin et al are presented above.

Regarding Claims 5 and 6 the combined references do not teach an array containing at least 1000 different CPG UNA oligonucleotides.

However Fodor et al teaches the concept of arrays which comprise a plurality of nucleic acid sequences attached to assigned locations on a solid substrate. Fodor et al teaches that there can be about 3000 different sequences on the array (Columns 2 and 3). Fodor teaches that this methodology provides a rapid, reliable, less expensive and

automatable means for reproducibly and accurately analyzing nucleic acid samples (Column 2).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have attached the probes of Laird to an array because the array methods of Fodor provides a rapid, reliable, less expensive and automatable means for reproducibly and accurately analyzing nucleic acid samples.

Regarding Claims 26-28 the combined references do not teach a kit containing an array of CPG UNA oligonucleotides.

However Fodor et al teaches the concept of packaging arrays in kits. Specifically Fodor et al teach that the kits contain various compartments with the desired necessary reagents, e.g., substrate, labeling reagents for target samples, buffers, and other useful accompanying products (Column 60). Additionally it would be obvious to include instructions on how to use the kit.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have packaged the array of probes into a kit. Reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time the invention was made. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the array of probes in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art wishing to perform hybridization reactions.

Conclusion

8. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634
May 30, 2006

CARLA J. MYERS
PRIMARY EXAMINER